a natural intracellular human c-IAP binding target, wherein said binding target is capable of specifically binding said human c-IAP, and

a candidate agent;

under conditions whereby, but for the presence of said candidate agent, said human c-IAP specifically binds said binding target at a reference affinity; and

detecting the binding affinity of said human c-IAP to said binding target to determine an agent-biased affinity,

wherein a difference between the agent-biased affinity and the reference affinity indicates that said candidate agent modulates a human c-IAP interaction with a natural c-IAP binding target.

16. (Amended) A method of inhibiting TNF-mediated apoptosis in a cell comprising the step of introducing into said cell a protein according to claim 10, 12 or 13 whereby said protein promotes or inhibits TNF-mediated apoptosis in said cell, wherein said method is performed in vitro.

REMARKS

Amendments

Claim 12 is amended to be dependent on claim 10 and to emphasize that the protein requires at least two of the three recited domains. Claims 14 and 16 are amended to remove reference to canceled claim 11. These amendments introduce no new matter.

Election/Restriction

Applicants confirm their election of Group I, and request rejoinder of duly limited method claims 13-16.

35USC112, first paragraph

Claims 10 requires a protein comprising residues 287-334 of SEQ ID NO:2. This sequence defines a novel third cIAP "BIR domain", which sequence is separately disclosed as SEQ ID NO:9.

The Specification teaches that the cIAP BIR domains represent novel protein-protein interaction domains and how multiple BIR domains can be mixed-and-matched in functional recombinant chimeras (e.g. Specification, p.12, lines 10-14). The Specification shows in experimental detail how to screen for interactions of such BIR domain containing proteins with proteins like TRAF (e.g. Specification, p.11, line 27 - p.14, line 13). Accordingly, the Specification conveys both possession and use of proteins comprising the specifically recited cIAP BIR domain.

Discerning and even practicing the invention does not require invoking Holy Grails or legendary knights of King Arthur; the invention does not relate to some hypothetical 3rd cIAP protein, nor does the invention require determining three dimensional molecular structures of anything. The present invention and relevant issues are much more mundane. A novel protein interaction domain is disclosed. The ability to recombine this domain into functional chimeric proteins is disclosed. And the claims are properly limited to a protein specifically comprising the novel interaction domain.

35USC112, second paragraph and *35USC102(e)*.

Claim 12, as amended to be dependent on claim 10 and to emphasize that the protein requires at least two of the three recited domains, is believed to be in compliance with the cited statutes.

The Examiner is invited to call the undersigned if he would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

We hereby petition for and authorize charging to our Deposit Account No. 19-0750 all necessary extensions of time. The Commissioner is hereby authorized to charge any fees or credit any overcharges relating to this communication to our Deposit Accnt No. 19-0750 (order no. T95-005-2).

Respectfully submitted,
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VERSION WITH MARKINGS TO SHOW CHANGES MADE

10. (Unamended) An isolated human cellular inhibitor of apoptosis protein (c-IAP) comprising the sequence set forth by residues 287-334 of SEQ ID NO:2.

12. (Amended) An isolated [human cellular inhibitor of apoptosis protein (c-IAP)] protein according to claim 10, comprising at least two of the following three domains: a first domain comprising SEQ ID NO: 5 or 6, a second domain comprising SEQ ID NO: 7 or 8, and a third domain comprising SEQ ID NO: 9 or 10.

13. (Unamended) An isolated protein according to claim 10 comprising SEQ ID NO:2.

14. (Amended) A method of screening for compounds which modulate a human c-IAP interaction with a c-IAP binding target, said method comprising the steps of:

incubating a mixture comprising:

a protein according to claim 10, [11,] 12, or 13,

a natural intracellular human c-IAP binding target, wherein said binding target is capable of specifically binding said human c-IAP, and

a candidate agent;

under conditions whereby, but for the presence of said candidate agent, said human c-IAP specifically binds said binding target at a reference affinity; and

detecting the binding affinity of said human c-IAP to said binding target to determine an agent-biased affinity,

wherein a difference between the agent-biased affinity and the reference affinity indicates that said candidate agent modulates a human c-IAP interaction with a natural c-IAP binding target.

15. (Unamended) A method according to claim 14, wherein said c-IAP binding target comprises a TRAF or fragment thereof sufficient to provide for c-IAP-specific binding.

16. (Amended) A method of inhibiting TNF-mediated apoptosis in a cell comprising the step of introducing into said cell a protein according to claim 10, [11,] 12 or 13 whereby said protein promotes or inhibits TNF-mediated apoptosis in said cell, wherein said method is performed in vitro.